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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/669,241	09/23/2003	Steffen Nock	020144-000520US	3544

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TOWNSEND AND TOWNSEND AND CREW, LLP
TWO EMBARCADERO CENTER
EIGHTH FLOOR
SAN FRANCISCO, CA 94111-3834

EXAMINER	
NAFF, DAVID M	

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 06/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/669,241	NOCK ET AL.	
	Examiner	Art Unit	
	David M. Naff	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-85* is/are pending in the application.

4a) Of the above claim(s) *36-59 and 61-85* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-35 and 60* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *23 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/23/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

A response of 3/22/06 to a restriction requirement of 2/22/06 elected Group I claims 1-35 and 60 with traverse.

The traverse requests that Group VI be combined with Group I since these are not independent inventions, and searching the claims of both groups will not be a serious burden since the claims of both groups are closely related by a common inventive concept that a peptide having an ester or thioester may be immobilized using an anchor molecule.

While the inventions of Groups I and VI require a peptide as asserted by applicants, the claims of the groups differ in other aspects. The claims of Group I require an anchor molecule comprising a first nucleophilic group at a 2 or 3 position relative to a second nucleophilic group, and attaching the anchor molecule to a surface. The claims of Group VI require an anchor molecule comprising a reactive group selected from a NH2-NH-R group and an aminooxy group, and do not require attaching the anchor molecule to a surface. Due to these differences, the claims of Groups I and VI require different inventions that are distinct and restrictable even through there is a relationship, and examining both inventions together will be a serous burden. The restriction requirement is still believed proper, and is adhered to and made final.

Claims 36-59 and 61-85 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely

traversed the restriction (election) requirement in the reply filed on 3/22/06.

Claims examined on the merits are 1-35 and 60.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-35 and 60 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are confusing and unclear as to the anchor molecule required by claims 1 and 60 defining the anchor molecule in terms of containing a first nucleophilic group at a 2 or 3 position relative to a second nucleophilic group. Being at a 2 or 3 position depends on the position chosen to be a 1 position, and this numbering of positions would be relative and subjective.

Claim 1 and claims dependent thereon, except for claim 2, are confusing and unclear how the intermediate compound in claim 1 can be formed without undergoing intramolecular rearrangement as required by claim 2. In view of the specification, the intermediate compound undergoes spontaneous rearrangement (page 16, line 3-5). Therefore, the intermediate compound is a transient compound that exists only for

an instant in a reaction to produce a bond between the anchor molecule and polypeptide. The specification discloses no way of stopping the reaction to prevent the intermediate compound from undergoing spontaneous rearrangement.

Claims 4 and 5 are unclear as to whether the 2-aminonucleophile or 3-aminonucleophile is the first or second nucleophilic group in claim 1.

In claim 33, the meaning and scope of "passive valve" (line 5) is uncertain.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35

U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-10, 15-17, 29-32 and 60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wagner et al (6,329,209 B1) in view of Kent et al (WO 96/34878) (both listed on 1449).

The invention is drawn to a method of immobilizing a polypeptide on a surface by contacting a polypeptide containing an ester or thioester with an anchor molecule containing a first nucleophilic group at a 2 or 3 position relative to a second nucleophilic group wherein the ester or thioester undergoes a trans-esterification reaction with the first nucleophilic group to form an intermediate compound which undergoes an intramolecular rearrangement in which the second nucleophilic group displaces the first nucleophilic group to form a stable bond between the anchor molecule and the polypeptide, and attaching the anchor molecule to a surface. The anchor molecule may contain an aminothiol as a nucleophilic group.

Wagner et al disclose attaching a protein-capture agent to a surface such as an organic thin film. The protein-capture agent can be a protein (col 4, line 54) such as a polypeptide (col 5, line 18), and can be bound an affinity tag non-covalently or covalently or as a fusion protein, and the affinity tag can covalently or non-covalently bond the protein-capture agent to the surface (col 9, lines 3-29). When the protein-capture agent and affinity tag are both proteins, the affinity tag may be attached to the protein-capture agent by intein-mediated protein ligation (col 22, line 30-31). The affinity tag may

be linked to the protein-capture agent via an adaptor (col 9, lines 30-39 and col 31, lines 19-24). The adaptor can be non-covalently or covalently attached to the affinity tag or protein-capture agent or both by chemical conjugation or as a fusion protein. The affinity tag, adaptor and protein-capture agent may be a fusion protein (col 23, lines 57-57).

Kent et al disclose protein synthesis by chemical ligation. As disclosed by page 7, lines 1-19 and page 8 (scheme 1), a peptide containing a thioester group is reacted with a peptide containing an N-terminal cysteine to form a linkage that spontaneously rearranges intramolecularly to form an amide bond linking the peptides. This ligation reaction is chemoselective to produce a native peptide bond at the ligation site.

It would have been obvious to attach the affinity tag of Wagner et al to the protein-capture agent using the ligation reaction of Scheme 1 of Kent et al to obtain the advantages of this reaction being chemoselective and providing a native peptide bond. The affinity tag is an anchor molecule since it attaches the protein-capture agent to the surface. It would have been obvious to provide the protein-capture agent with an thioester group since the capture agent can be a protein, polypeptide or peptide and it would have been obvious to provide the affinity tag with an N-terminal cysteine group since the affinity tag can be an amino acid, poly(amino acid) or protein. The conditions of dependent claims would have been matters of obvious choice within the ordinary skill of the art in view of the disclosures

of the references. Wagner et al disclose (col 38, lines 39-61) a chip of the type required by claims 28-31.

Claim Rejections - 35 USC § 103

Claims 11-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over the references as applied to claims 1-10, 15-17, 29-32 and 60 above, and further in view of Chong et al (AJ on 1449) or IMPACT CN System (892).

The claims require the anchor molecule to contain a tag moiety such as a chitin binding domain that can be noncovalently bonded to a molecule attached to the surface.

Chong et al disclose using a chitin binding domain as an affinity tag to purify a recombinant protein.

IMPACT CN System discloses using a chitin binding domain to purify a protein on a chitin column.

When attaching the affinity tag of Wagner et al to a polypeptide protein-capture agent as set forth above, it would have been obvious to provide the affinity tag of Wagner et al with a chitin binding domain to noncovalently bind the tag to the surface since Wagner et al can use noncovalent bonding as an alternative to covalent bonding of the tag to the surface and since Chong et al or IMPACT CN System would have suggested the function of the chitin binding domain to noncovalently bind.

Claim Rejections - 35 USC § 103

Claims 18-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over the references as applied to claims 1-10, 15-17, 29-

32 and 60 above, and further in view of Wu et al (AN on 1449) and IMPACT CN System.

The claims require forming the polypeptide containing the ester or thioester by expressing a gene that encodes a fusion protein containing a polypeptide and an intein joined to the polypeptide at a spice junction at the amino terminus of the intein having a carboxyl terminus lacking a functional splice junction, and contacting the fusion protein with a nucleophilic compound that releases the polypeptide from the intein at the splice junction to form the polypeptide containing a terminal ester or thioester.

Wu et al disclose protein trans-splicing by a split intein encoded in a split DnaE gene of *Synechocystis sp.* PCC6803. The DnaE protein of *Synechocystis sp.* PCC6803 is encoded by a split gene interrupted by intein sequences.

IMPACT CN System disclose cleavage of an intein to release a target protein from a chitin-bound intein tag.

When using a polypeptide containing a thioester as the protein-capture agent of Wagner et al as set forth above, it would have been obvious to use the DnaE gene of *Synechocystis sp.* PCC6803 to produce the polypeptide containing the thioester as suggested by Wu et al since IMPACT CN System would have suggested that cleavage of an intein can be used to release a bound protein.

Claim Rejections - 35 USC § 103

Claim 33-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over the references as applied to claims 1-10, 15-17, 29-

32 and 60 above, and further in view of Brown et al (5,807,522) (listed on 1449).

The claims require placing the polypeptide in contact with the surface using a microvolume dispenser comprising a body, at least one vertical channel in the body and an interior surface of the channel being hydrophobic.

Brown et al disclose the use of a capillary dispenser to provide a defined volume of liquid on a support in producing microarrays of biological samples on a support.

It would have been obvious to use the dispenser of Brown et al to apply the polypeptide protein-capture agent of Wagner et al ('209) onto a surface when attaching the polypeptide to the surface using the reaction of Kent et al as set forth above.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David M. Naff whose telephone number is 571-272-0920. The examiner can normally be reached on Monday-Friday 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David M. Naff
Primary Examiner
Art Unit 1651

DMN
7/8/06